REMARKS

Claims 1-10 have been cancelled without prejudice, disclaimer or admission. Claims 24-33 have been added and consideration of these claims is respectfully requested. An appendix captioned "Version with markings to show changes made" depicting changes made to the claims is attached hereto for the Examiner's convenience.

Favorable consideration of the following remarks as they pertain to the newly pending claims is respectfully requested.

Rejections Under 35 U.S.C. §102

Claims 1, 2, 6-10 stand rejected under 35 U.S.C. §102(a) as being anticipated by WO 9905175. In addition, these claims stand rejected under 35 U.S.C. §102(b) as being anticipated by Myers. Applicants respectfully traverse.

As a preliminary matter, Applicants point out that Claims 1, 2, and 6-10 have been cancelled without prejudice, disclaimer or admission.

The Office Action expresses that WO 9905175 teaches a nucleic acid sequence having about 41% homology to the instant SEQ ID NO:1.

Myers discloses a 399 nucleotide sequence having 99% identity to nucleotides 171-573 of SEQ ID NO:1, but an overall identity to SEQ ID NO:1 of less than 16%.

In contrast, the newly pending claims are drawn to nucleic acids comprising nucleic acid sequences having at least about 95% identity to the full length nucleic acid sequence set forth in SEQ ID NO:1, and nucleic acids encoding amino acid sequences having at least about 95% identity to the full length amino acid sequence set forth in SEQ ID NO:2.

Applicants submit that new Claims 24-33 are drawn to nucleic acids distinct from those disclosed by WO 9905175 and Myers. Accordingly, Applicants submit that WO 9905175 and Myers do not anticipate the invention set forth by Claims 24-33, and respectfully request withdrawal of the rejection and allowance of the claims.

Rejections Under 35 U.S.C. §112, - Enablement

Claims 1-10 stand rejected under 35 U.S.C. §112 as lacking enablement. Applicants respectfully traverse.

As a preliminary matter, Applicants point out that Claims 1-10 have been cancelled without prejudice, disclaimer or admission. The new claims 24-33 are drawn to recombinant nucleic acids, expression vectors, host cells comprising recombinant nucleic acids, and processes for making Mkinase protein using such host cells. Among other uses, the compositions find utility in screening assays for binding partners and/or modulators of Mkinase.

The Examiner's main point seems to be that while Mkinase is capable of binding to Traf4, the function of Traf4 is uncertain and the way to use Mkinase is accordingly not clear. Applicants respectfully disagree.

As acknowledged by the Examiner, the instant Mkinase protein is capable of binding to Traf4 and comprises a kinase domain with homology to MAP kinases and CDK families, which are known to be involved in the regulation of cell proliferation. Regarding the function of Traf4, the Examiner acknowledges that the expression of Traf4 is altered in several cancer cell types; upregulation of Traf4 being reported in some cancers and downregulation being reported in others. Such findings support that Traf4 regulation is important for normal cell division. In addition, Applicants point out that the Traf4 gene was previously identified as being amplified in human primary breast cancer (Bieche et al., Cancer Res. 56:3886-3890, 1996). Further, Traf4 has also been shown to be required for normal cell growth during development (Shiels et al., Am. J. Pathol, 157:679-688, attached as Exhibit A). More recently, the Traf4 gene has also been shown to be downstream of the PTEN tumor suppressor gene (Matsushima-Nishiu et al., Cancer Res. 61:3741-3749, 2001), further implicating the Traf4 protein in the regulation of cell proliferation.

Accordingly, due to the role of homologous kinase proteins in the regulation of cell division, the binding of Mkinase to Traf4, and the involvement of Traf4 in cell division, Applicants submit that the artisan of reasonable skill would know how to use the claimed compositions to test for modulators of cell division.

The Examiner's attention is respectfully drawn to the Utility Examination Guidelines, Federal Register, Vol.66, No.4, page 1098:

> Any rejection based on lack of utility should include a detailed explanation why the claimed invention has no specific and substantial credible utility. Whenever possible, the examiner should provide documentary evidence regardless of publication date . . . to support the factual basis for the prima facie showing of no specific and substantial credible utility.

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. . . The prima facie showing must contain the following elements:
(1) An explanation that clearly sets forth the reasoning used in concluding that the asserted utility for the claimed invention is not both specific and substantial nor well-established;
(2) Support for factual findings relied upon in reaching this conclusion; and
(3) An evaluation of all relevant evidence of record, including utilities taught in the closest prior art.

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A rejection based on lack of utility should not be maintained if an asserted utility for the claimed invention would be considered specific, substantial and credible by a person of ordinary skill in the art in view of all the evidence of record.

Office personnel are reminded that they must treat as true a statement of fact made by an applicant in relation to an asserted utility, unless countervailing evidence can be provided that shows that one of ordinary skill in the art would have a legitimate basis to doubt the credibility of such a statement.

Applicants submit that the claimed Mkinase compositions have specific, real world, credible utility. Applicants further submit that the artisan of reasonable skill would know how to use the claimed compositions to screen for modulators likely to affect the cell cycle. Accordingly, Applicants request withdrawal of the rejection and allowance of the new claims.

Rejections Under 35 U.S.C. §112 - Written Description

Claims 1, 4 and 6-10 stand further rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a manner as to reasonably convey that the Applicants had possession of the claimed invention at the time the application was filed. Basically, the Examiner objects to the use of the term "cell cycle protein". The claims have been amended to recite Mkinase proteins comprising specific

sequences as well as the ability to bind to Traf4; accordingly the rejection should be withdrawn.

Rejections Under 35 U.S.C. §112 - Indefinite

Claims 1, 2 and 6-10 stand rejected under 35 U.S.C. §112, second paragraph, as being indefinite for use of the phrase "hybridizing under high stringency conditions".

As a preliminary matter, Applicants point out that Claims 1, 2 and 6-10 have been cancelled without prejudice, disclaimer or admission. In addition, Applicants point out that new Claims 24-33 do not recite nucleic acids that hybridize under high stringency conditions. The new claims recite Mkinase proteins comprising specific sequences as well as the ability to bind to Traf4.

Applicants submit that the newly pending claims avoid the Examiner's rejection, and respectfully request withdrawal of the rejection and allowance of the claims.

CONCLUSION

Applicants submit that the application is now in form for allowance and early notification of such is requested. If there remain issues that the Examiner believes may be resolved by telephone, he is respectfully requested to contact the undersigned at (415) 781-1989.

Respectfully submitted,

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Version with markings to show changes made

In the specification:

~~Cell cycle proteins of the present invention may be shorter or longer than the amino acid sequence encoded by the nucleic acid shown in the Figure. Thus, in a preferred embodiment, included within the definition of cell cycle proteins are portions or fragments of the amino acid sequence encoded by the nucleic acid sequence provided herein. In one embodiment herein, fragments of cell cycle proteins are considered cell cycle proteins if a) they share at least one antigenic epitope; b) have at least the indicated sequence identity; c) and preferably have cell cycle biological activity as further defined herein. In some cases, where the sequence is used diagnostically, that is, when the presence or absence of cell cycle protein nucleic acid is determined, only the indicated sequence identity is required. The nucleic acids of the present invention may also be shorter or longer than the sequence in the Figure. The nucleic acid fragments include any portion of the nucleic acids provided herein which have a sequence not exactly previously identified; fragments having sequences with the indicated sequence identity to that portion not previously identified are provided in an embodiment herein.~~

~~In addition, as is more fully outlined below, cell cycle proteins can be made that are longer than those depicted in the Figure; for example, by the addition of epitope or purification tags, the addition of other fusion sequences, or the elucidation of additional coding and non-coding sequences. As described below, the fusion of a cell cycle peptide to a fluorescent peptide, such as Green Fluorescent Peptide (GFP), is particularly preferred.~~

~~Cell cycle proteins may also be identified as encoded by cell cycle nucleic acids which hybridize to the sequence depicted in the Figure, or the complement thereof, as outlined herein. Hybridization conditions are further described below.~~

Cell cycle proteins of the present invention may be shorter or longer than the amino acid sequence encoded by the nucleic acid shown in the Figure 1 (SEQ ID NO:1). Thus, in a preferred embodiment, included within the definition of cell cycle proteins are portions or fragments of the amino acid sequence encoded by the nucleic acid sequence provided herein. In one embodiment herein, fragments of cell cycle proteins are considered cell cycle proteins if a) they share at least one antigenic epitope; b) have at least the indicated sequence identity; c) and preferably have cell cycle biological activity as further defined herein. In some cases, where the sequence is used diagnostically, that is, when the presence or absence of cell cycle protein nucleic acid is determined, only the indicated sequence identity is required. The nucleic acids of the present invention may also be shorter or longer than the sequence in Figure 1 (SEQ ID NO:1). The nucleic acid fragments include any portion of the nucleic acids provided herein which have a sequence not exactly previously identified; fragments having sequences with the indicated sequence identity to that portion not previously identified are provided in an embodiment herein.

In addition, as is more fully outlined below, cell cycle proteins can be made that are longer than those depicted in Figure 2 (SEQ ID NO:2); for example, by the addition of epitope or purification tags, the addition of other fusion sequences; or the elucidation of additional

coding and non-coding sequences. As described below, the fusion of a cell cycle peptide to a fluorescent peptide, such as Green Fluorescent Peptide (GFP), is particularly preferred.

Cell cycle proteins may also be identified as encoded by cell cycle nucleic acids which hybridize to the sequence depicted in Figure 1 (SEQ ID NO:1), or the complement thereof, as outlined herein. Hybridization conditions are further described below.

In the Claims:

~~1. A recombinant nucleic acid encoding a cell cycle protein comprising a nucleic acid that hybridizes under high stringency conditions to a sequence complementary to that set forth in Figure 1.~~

~~2. The recombinant nucleic acid of claim 1 wherein said protein binds to Traf4~~

~~3. The recombinant nucleic acid of claim 1 comprising a nucleic acid sequence as set forth in Figure 1.~~

~~4. A recombinant nucleic acid encoding a cell cycle protein comprising a nucleic acid having at least 85% sequence identity to a sequence as set forth in Figure 1.~~

~~5. A recombinant nucleic acid encoding an amino acid sequence as shown in Figure 2.~~

~~6. An expression vector comprising the recombinant nucleic acid according to any one of claims 1, 2, 3, 4, or 5, operably linked to regulatory sequences recognized by a host cell transformed with the nucleic acid.~~

~~7. A host cell comprising the recombinant nucleic acid according to any one of claims 1, 2, 3, 4, or 5.~~

~~8. A host cell comprising the vector of claim 6.~~

~~9. A process for producing a cell cycle protein comprising culturing the host cell of claim 8 under conditions suitable for expression of a cell cycle protein.~~

~~10. A process according to claim 9 further comprising recovering said cell cycle protein.~~

24. A recombinant nucleic acid encoding a Mkinase protein, comprising a nucleic acid sequence having at least about 95% identity to the full length nucleic acid sequence set forth in SEQ ID NO:1, wherein said Mkinase protein binds to a Traf4 protein.

25. A recombinant nucleic acid encoding a Mkinase protein, comprising the nucleic acid sequence set forth in SEQ ID NO:1.

26. A recombinant nucleic acid encoding a Mkinase protein, which protein comprises an amino acid sequence having at least about 95% identity to the full length amino acid sequence set forth in SEQ ID NO:2, wherein said Mkinase protein binds to a Traf4 protein.

27. A recombinant nucleic acid encoding a Mkinase protein, wherein said Mkinase comprises the amino acid sequence set forth in SEQ ID NO:2.

28. A recombinant nucleic acid according to Claim 24, 25, 26, or 27, further comprising a fusion partner.

29. An expression vector, comprising a recombinant nucleic acid according to any one of Claims 24-27 operably linked to a regulatory sequences recognized by a host cell transformed with the nucleic acid.

30. A host cell comprising a nucleic acid according to any one of Claims 24-27.

31. A host cell comprising an expression vector according to Claim 29.

32. A process for producing a Mkinase protein, comprising culturing a host cell according to Claim 30 or 31 under conditions suitable for expression of said Mkinase protein.

33. A process according to Claim 32, further comprising recovering said Mkinase protein.